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Sudden Cardiac Death in Young Athletes

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Abstract

Introduction: Physical exercise is recommended to everyone, however, some individuals, due to their genetics and physiology, are at risk of suffering from sudden death (SD) while practicing sports and the most frequent cause is sudden cardiac death (SCD). Although SCD is not common among young athletes, when it happens is an event with huge emotional impact in the community.

Objectives: To develop a bibliographic review of the main causes of SCD and to present an evaluation algorithm based on current recommendations and guidelines.

Methods: Bibliographic review of documents published between 2006-2018 in PubMed, European Society of Cardiology, American Heart Association and American College of Cardiology focusing the main causes of SCD in the athlete complemented with the research of algorithms recommended, at European and American level.

Results: The risk of SCD in young individuals ranges from 0.5 to 3.7 events per 100.000 person/year and exercise acts as a precipitation factor. The most common causes are cardiomyopathies (hypertrophic cardiomyopathy (HCM) and arrhythmogenic right ventricular dysplasia (ARVD)) and coronary artery anomalies. It is difficult to identify these conditions, since they may not be clinically apparent and may first present with SD. Therefore, identification of risk factors, such as symptoms related to arrhythmia, medications used to improve physical performance and family history of cardiac conditions is of highly importance, as they can alert to a potentially fatal cardiac condition.

Conclusions: The main causes have already been identified, but the problem remains the difficulty of the diagnosis: most diseases are indolent, the first manifestation is often SD and there is no consensus on how to select athletes that can take part in sports and those who should be recommended to avoid practicing. The algorithm presented is a synthesis of current recommendations and guidelines aimed to help the physician to better decide regarding exercise practice.

MESH Words: Sudden Death; Sudden Cardiac Death; Young Athlete

Resumo

Introdução: O exercício físico é recomendado universalmente, contudo, alguns indivíduos, devido à sua genética e fisiologia, estão em risco de morte súbita durante a prática de exercício, sendo a principal causa cardíaca. Apesar de não ser comum entre os jovens atletas, quando ocorre, é um evento com elevado impacto emocional em toda a comunidade.

Objetivos: Desenvolver uma revisão bibliográfica sobre as principais causas de morte súbita cardíaca e apresentar um algoritmo de avaliação baseado nas recomendações e *guidelines* atuais.

Métodos: Revisão bibliográfica baseada em documentos publicados entre 2006-2018 nas bases de dados: *PubMed*, *European Society of Cardiology*, *American Heart Association e American College of Cardiology*, sobre as principais causas de morte súbita cardíaca em atletas, complementado com a pesquisa de algoritmos recomendados, tanto a nível Europeu como Americano.

Resultados: O risco de morte súbita cardíaca em jovens varia entre 0.5 e 3.7 por 100.000 pessoas/ano e o exercício atua como fator precipitante. As causas mais comuns são miocardiopatias (miocardiopatia hipertrófica e a displasia arritmogénica do ventrículo direito) e anomalias coronárias. Estas condições são difíceis de identificar e a sua primeira manifestação é frequentemente a morte súbita. Assim sendo, a identificação de fatores de risco, como sintomas relacionados com arritmia, uso de determinados fármacos e história familiar de doenças cardíacas é de extrema importância porque podem alertar para uma alteração cardíaca potencialmente fatal.

Conclusões: As principais causas de morte súbita cardíaca já foram identificadas, mas o problema consiste na dificuldade do diagnóstico: a maioria das doenças são indolentes, a primeira manifestação é frequentemente a morte súbita e não há consenso sobre qual a melhor maneira de selecionar os atletas que poderão praticar exercício e aqueles em que deve ser evitado. O algoritmo apresentado é uma síntese das *guidelines* atuais, direcionado a auxiliar a decisão do médico relativamente à prática de exercício.

MESH Words: Sudden Death; Sudden Cardiac Death; Young Athlete

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Resumo Alargado

O exercício físico é recomendado universalmente, contudo, alguns indivíduos, devido à sua genética e fisiologia, estão em risco de morte súbita durante a prática de exercício, sendo a principal causa cardíaca. Apesar de não ser comum entre os jovens atletas, quando ocorre, é um evento com elevado impacto emocional em toda a comunidade. De forma a prevenir estes eventos, é necessária a identificação de fatores de risco que possam alertar para uma condição potencialmente fatal e uma correta recomendação relativamente à prática ou evicção de exercício físico.

Como tal, os objetivos deste trabalho consistem em desenvolver uma revisão bibliográfica sobre as principais causas de morte súbita de causa cardíaca e apresentar um algoritmo de avaliação baseado nas recomendações e *guidelines* atuais.

Foi realizada uma revisão bibliográfica baseada em documentos publicados entre 2006 e 2018 nas bases de dados: PubMed, European Society of Cardiology, American Heart Association e American College of Cardiology, sobre as principais causas de morte súbita cardíaca em atletas, complementado com a pesquisa de algoritmos recomendados atualmente, tanto a nível Europeu como Americano.

A morte súbita é um evento fatal, inesperado e não traumático, que ocorre dentro de 1 hora após o início dos sintomas, num indivíduo aparentemente saudável. A causa médica mais comum de morte súbita é a cardíaca.

Em termos epidemiológicos, as estimativas variam bastante com base na população estudada, estando condicionados pela idade dos atletas, a intensidade do exercício que praticam e o tipo de desporto em que estão envolvidos.

No entanto, há uma clara predominância dos eventos no sexo masculino, com uma relação de aproximadamente 5:1 e um aumento significativo do risco nos atletas de origem Africana.

A morte súbita em jovens (considerados <35 anos) é um evento pouco comum, estimando-se a ocorrência de 0,5 a 3,7 eventos por 100.000 jovens/ano.

Os fatores de risco que devem despertar atenção para uma possível anomalia cardíaca, potencialmente causadora de morte súbita são: Sintomas relacionados com arritmia, a existência de patologia cardíaca, fatores de risco cardiovasculares, consumo de determinados fármacos e história familiar de morte súbita ou paragem cardíaca.

Em termos etiológicos, há uma clara diferença entre os jovens e os mais velhos. Nos últimos, a principal causa é a doença coronária, sendo a aterosclerose responsável por mais de metade dos eventos de morte súbita em atletas com mais de 35 anos. Já nos jovens, há um predomínio de miocardiopatias, sendo a principal causa a miocardiopatia hipertrófica, responsável por 36% das mortes.

A miocardiopatia hipertrófica é uma doença do miocárdio, de transmissão hereditária autossómica dominante, que se caracteriza por hipertrofia do ventrículo esquerdo. Estima-se que afete 1 em 500 indivíduos e pode manifestar-se em qualquer idade. A sua expressão clínica pode variar desde assintomática a morte súbita, sendo que o risco desta atinge um pico entre os 8 e os 16 anos. Os fatores que devem levantar a suspeita para esta etiologia são: paragem cardíaca prévia, síncope inexplicada, história familiar de morte súbita, hipertrofia ventricular esquerda marcada, taquicardia ventricular e diminuição da pressão arterial em resposta ao exercício. O diagnóstico deve ser realizado por ecografia ou ressonância magnética, através da identificação de hipertrofia do ventrículo esquerdo. Já foram descritas mortes por HCM em atletas em competição, mas também durante atividades recreativas, o que indica que nem mesmo a total restrição de exercício físico permita prevenir as mortes por esta causa.

A Displasia Arritmogénica do Ventrículo Direito é uma doença de transmissão hereditária autossómica dominante, com penetrância incompleta e com prevalência estimada entre 1 em 1000 a 1 em 5.000 indivíduos, apresentando predileção pelo sexo masculino. Surge por mutações nos genes que codificam as proteínas desmossómicas cardíacas, provocando uma substituição do tecido muscular por tecido fibro-adiposo, afetando particularmente o VD, o que aumenta o risco de morte súbita por taquicardia ou fibrilhação ventricular. A doença manifesta-se maioritariamente entre a 2ª e a 5ª década de vida, através de palpitações, sincope e paragem cardíaca súbita, particularmente no atleta. O exercício físico, para além de estar associado ao aparecimento mais precoce de manifestações da doença, também acelera a expressão fenotípica da doença e aumenta o risco de arritmia ventricular. A adaptação do ventrículo direito ao exercício num atleta pode mimetizar a doença, surgindo uma ‘*’grey area*’’ entre o que é considerado uma adaptação fisiológica e o fenótipo da doença, dificultando o diagnóstico. Segundo os estudos, existe um risco 5x superior de morte por ARVD em atletas em comparação com não atletas.

As anomalias coronárias são modificações da origem, do curso ou da estrutura. Tem uma incidência estimada entre 0,2% e 5,6% na população geral e são na maioria das casos anomalias assintomáticas, quando sintomáticas manifestam-se por dor torácica ou dispneia durante o esforço, no entanto, a primeira manifestação pode ser a morte súbita, o que acontece em aproximadamente 50% dos casos, sem qualquer sintoma prévio. A anomalia congénita mais comum corresponde a uma origem da artéria coronária do seio de valsava oposto, com um percurso interarterial. Normalmente não são detetadas durante a vida, contudo, durante o exercício intenso, há um aumento das necessidades de O2 com uma redução do período diastólico que, combinado a uma diminuição da perfusão do miocárdio por estreitamento coronário e estreitamento adicional provocado pelo estado dinâmico da aorta pode despoletar isquemia miocárdica, arritmia ventricular e morte súbita. O melhor método de diagnóstico é a angiografia coronária.

Relativamente às anomalias adquiridas, a principal causa é a doença de Kawasaki. Trata-se de uma vasculite de pequenos e médios vasos, que pode causar inflamação do miocárdio. Afeta predominantemente crianças até aos 5 anos, mas as sequelas podem estender-se à vida adulta provocando fibrilhação ventricular e enfarte do miocárdio, que são a causa de morte súbita nos atletas.

A disseção aórtica é uma causa pouco comum de morte súbita em atletas, estando em risco de sofrer desta patologia os pacientes com doenças que causem enfraquecimento da parede ascendente da aorta e predisponham a dilatação patológica durante períodos de stress prolongado: a causa mais frequente é a síndrome de Marfan.

A síndrome de Marfan corresponde a um defeito no gene que codifica a fibrilina-1, uma proteína do tecido elástico presente no coração e nos vasos sanguíneos, cuja alteração causa enfraquecimento do tecido, predispondo à dilatação. Durante o exercício intenso ocorre um aumento da pressão arterial e stress sobre a aorta que acelera a formação de aneurismas e aumenta o risco de disseção aórtica. As alterações cardíacas podem ser identificadas através de ecografia, TC ou ressonância, pela medição da raiz da aorta.

O estudo pré-competição aparenta ser eficaz na prevenção de morte súbita, dado que permitiu diminuir o número de eventos fatais durante a prática desportiva, no entanto, o protocolo de avaliação varia entre a Europa e os EUA: Na Europa é recomendado o estudo de atletas envolvidos em desportos de alta intensidade, aqueles que participam em desportos de intensidade baixa não requerem avaliação pré-competição e os que

participam em desportos de media intensidade deve fazer uma autoavaliação do risco e apenas se considerarem ser positivo, então devem ser avaliados por um médico. Consoante esse avaliação inicial, ou são autorizados a praticar desporto ou serão submetidos a exames de diagnóstico adicionais. Quanto às *guidelines* americanas, preconizam uma *checklist* pré-participação a todos os atletas e caso haja alterações, então uma avaliação adicional é recomendada, no entanto reconhecem que não será custo-efetivo, porque a lista de atletas a rastrear é muito grande, comparada ao número de atletas que irão necessitar de avaliação subsequente.

De forma a fazer uma melhor avaliação do risco do atleta e para uma correta recomendação para a prática desportiva é apresentado um algoritmo que sintetiza as recomendações encontradas nas *guidelines* Americanas e Europeias.

Em suma, a morte súbita é um evento traumático que, por afetar uma população jovem e aparentemente saudável, tem um enorme impacto na comunidade. As principais causas já foram identificadas, mas o problema mantém-se a dificuldade do diagnóstico: a maioria das doenças são indolentes, a primeira manifestação é frequentemente a morte súbita e não há consenso sobre qual a melhor maneira de selecionar os atletas que poderão praticar exercício físico e aqueles em que deve ser evitado.

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Acronyms List

AAD Acute Aortic Dissection

ACC American College of Cardiology

AHA American Heart Association

ARVD Arrhythmogenic Right Ventricular Dysplasia

CA Coronary Angiography

CAD Coronary Artery Disease

CCAA Congenital Coronary Artery Anomalies

ECG Electrocardiogram

ESC European Society of Cardiology

HCM Hypertrophic Cardiomyopathy

ICD Implantable Cardiac Defibrillator

KD Kawasaki Disease

LV Left Ventricle

LVH Left Ventricular Hypertrophy

MESH Medical Subject Headings

MR Magnetic Resonance

RV Right Ventricle

SCA Sudden Cardiac Arrest

SCD Sudden Cardiac Death

SD Sudden Death

SIDS Sudden Infant Death Syndrome

CT Computed Tomography

VF Ventricular Fibrillation

VT Ventricular Tachycardia

Introduction

It is known that physical exercise is recommended to everyone due to its health benefits. However, in specific cases, it can have devastating results as it is the case of athletes who, due to their genetics and physiology, are at risk of suffering from sudden death (SD) while practicing sports. The death of an athlete, that is both young and presumably healthy, causes a large emotional and social impact on the surrounding community.

SD is a non-traumatic, unexpected fatal event occurring within 1 hour of the onset of symptoms in an apparently healthy subject. The term Sudden Cardiac Death (SCD) applies when the cause of SD was a congenital or acquired cardiac condition potentially fatal already known or identified during the autopsy.[1]

The risk of SCD is higher in men than in women, and it increases with age due to the higher prevalence of coronary artery disease (CAD) in older people. The rate is estimated to range from 1,40 per 100.000 person/year in women to 6,68 per 100.000 person/year in men. SCD in younger individuals (≤35 years) has an estimated incidence of 0,5 to 3,7 events per 100.000 person/year, corresponding to a rough estimate of 1100–9000 deaths in Europe and 800–6200 deaths in the USA every year.[1,2]

Cardiac diseases associated with SCD differ in young vs. older individuals. In older populations, chronic degenerative diseases predominate (CAD, valvular heart diseases and hearth failure). In the young there is a predominance of cardiomyopathies and channelopathies, as well as myocarditis and substance abuse. [1,3] In the young athletes, cardiomyopathy has been demonstrated as the most common cause of exercise-related SCD. [4] It results from intense physical exercise in the context of an underlying silent cardiovascular abnormality, and the first manifestation is often sudden death.

Prevention of SCD requires identification of risk factors that can alert to a potentially fatal cardiac condition. The problem underlies on the difficulty of the diagnosis since it is recommended that people who practice sports undertake periodic screenings in order to evaluate potential risks, but there is no consensus on the most effective and efficient way to accomplish it. [5]

The main causes of SCD will be reviewed and an evaluation algorithm will be presented, based on the existing knowledge of the subject, in order to identify risk factors for SCD and to better advise on the permanency or interruption of sports practice, particularly at a competitive level.

Material Selection

Eligibility criteria

Clinical practice guidelines and consensus documents were included. The search included articles where recommendations were proposed supported by scientific literature and excluded reviews and opinion articles based on the opinion of a single author. The search strategy was restricted to studies beginning in 2006.

Bibliographical sources and search strategy

Bibliographic sources used were selected from the following databases: PubMed, European Society of Cardiology (ESC), American Heart Association (AHA) and American College of Cardiology (ACC).

The research was adapted to the particularities of each database. Medical Subject Headings (MESH) and keywords: (1) Sudden Cardiac Death and (2) Young Athletes.

It was also developed a research based on bibliographical references of the recommendations that were being found in order to find potentially eligible articles.

Selection of documents

The documents were evaluated from their titles and summaries. Those that were considered potentially eligible for inclusion were obtained in full text.

Outcomes and prioritization

The main objective is to perform the current revision of the theme and the secondary objective to propose an evaluation algorithm.

Structuring of results

A bibliographic review was done on the subject, focusing on the main causes of SCD in the athlete complemented with the research of algorithms currently recommended, both at European and American level.

Epidemiology of Sudden Cardiac Death

SCD is the most frequent medical cause of SD in athletes, and estimates vary widely based on the population and the definition, since some estimates of incidence include only deaths with exertion or shortly (< 1 hour) after exertion, while others include any SCD in an athlete (exertional or outside of exertion). [6] The annual incidence of SCD in young athletes is estimated to range from 0,5 to 3,7 per 100.000 athletes. [1,2,7]

By analysing the data from the studies there are characteristics which are more associated with SCD: there is a significant sex predominance, with males (6.68 /100.000) having 5 times more incidence of SCD than females (1,4/100.000). In terms of ethnic groups, the African athletes have a higher incidence rate (5,6/100.000 per year) in the USA.[4]

The intensity of the activity and the age of the athletes are core risk factors.[1] The sport type also seems to be a predictive factor. In Europe, football has the greatest incidence, while in USA basketball and the American football predominate. This suggests that individuals participating in sports of high dynamic and low isometric intensity are at higher risk of death. [4]

Risk Factors for SCD in young athletes

Although SCD is not common among young athletes, exercise is a precipitation factor for its occurrence and if any of the following risk factors are presented, it is necessary a careful evaluation in order to reduce the probability of a fatal event.[8]

1. Symptoms/events related to arrhythmia
    a. Palpitations;
    b. Light-headedness;
    c. Syncope;
    d. Dyspnea;
    e. Chest pain;
    f. Cardiac arrest;
2. Known heart disease (congenital or acquired)
3. Risk factors for heart disease
    a. Hypertension;
    b. Diabetes Mellitus;
    c. Hyperlipidemia;
    d. Smoking;

4. Medications:
    a. Antiarrhythmic medications;
    b. Other medications with potential for QT prolongation and torsades de pointes;
    c. Medications with potential to provoke or aggravate ventricular arrhythmias;
    d. Stimulants including cocaine and amphetamines
    e. Supplements including anabolic steroids;
5. Family History
    a. SCD, Sudden Cardiac Arrest (SCA), or unexplained drowning in a first-degree relative;
    b. Sudden Infant Death Syndrome (SIDS) or repetitive spontaneous pregnancy losses given their potential association with cardiac channelopathies;

Etiology

According to studies, in athletes older than 35 years, 80% of SCD is due to atherosclerotic coronary artery disease, but in younger athletes inherited cardiac conditions predominate: cardiomyopathies (such as HCM and ARVD) and coronary artery anomalies are the most common causes of SCD in young athletes, other less significant causes are ion channelopathies (Long QT Syndrome, Brugada syndrome, catecholaminergic polymorphic ventricular tachycardia), atherosclerotic coronary artery disease and aortic dissection and rupture. [4,6,9]

In the US, the National Registry of Sudden Death in Athletes was established at the Minneapolis Heart Institute in the 1980s and has reported on 1866 sudden deaths in individuals practicing sports, in a 27-year observational period. Their data show that 36% of all sudden deaths in this registry are attributed to confirmed cardiovascular causes, of which the most frequent are HCM (36%), congenital anomalies of the coronary arteries (17%), myocarditis (6%), ARVD (4%) and channelopathies (3.6%).[10] In older athletes, as in the general population, coronary atherosclerotic disease accounts for more than half of cases.[11]

It is also notable that reports from other countries such as Italy and Denmark have found that the most common cause of SCD in young athletes is ARVD, responsible for around 25% of SCD cases in athletes from those countries. [6]

Many of these diagnoses may not be clinically apparent and may first present with sudden death. Approximately 30% of athletes with SCD have been reported to have had symptoms such as chest pain, shortness of breath, performance decline, palpitations, pre-syncope, or syncope leading up to the event. Evaluation of such exertional symptoms by a qualified team of sports medicine and cardiology physicians is an important aspect of the medical care of athletes and of SCD prevention. [6]

Hypertrophic Cardiomyopathy

HCM is the most commonly identified cause for SCD in the young, including competitive athletes. [6,12]

HCM is a primary myocardial disorder, typically with an autosomal dominant pattern of inheritance, characterized by left ventricular hypertrophy (LVH), in the absence of abnormal loading conditions, and myocardial disarray on histology. [4] In the general population, the estimated prevalence of hypertrophic cardiomyopathy is 1:500. [12,13,14] At least 27 HCM-susceptibility genes have been implicated to date, with hundreds of mutations identified. Sarcomeric or myofilament HCM is the most common HCM genetic subtype, due to mutations in genes encoding for proteins of the thick and thin myofilaments of the cardiac sarcomere. The two most common HCM-associated genes, MYBPC3 and MYH7, have an estimated prevalence of 25% to 35% for each gene and account for the majority of research based positive genetic tests.[13]

Phenotypic expression of hypertrophic cardiomyopathy may first occur at all phases of life, from infancy to old age. The clinical spectrum of hypertrophic cardiomyopathy is quite diverse, ranging from a completely asymptomatic state to symptoms related to outflow tract obstruction, diastolic dysfunction, progressive heart failure, various tachyarrhythmias, and sudden cardiac death, which is often the first clinical manifestation. [12]

Three distinctive modes of hypertrophic cardiomyopathy-related death – heart failure, stroke, and sudden cardiac death – occurring largely during different periods of life have been reported. [12, 13] The risk of sudden death during infancy is low (between 2 and 7 years of age), but it peaks in the 8 to 16 year-old age group; in adolescents and adults, most of sudden death events are attributable to ventricular tachyarrhythmias – ventricular tachycardia and ventricular fibrillation, probably due to the interaction of catecholamines, metabolic acidosis, dehydration, contracted blood volume, and electrolyte abnormalities with the pathological substrates of disorganised myocyte alignment and microvascular ischaemia – and usually occur in the presence of ≥1 of the major risk markers: 1) previous cardiac arrest 2) unexplained syncope; 3) family history of SCD; 4) severe LVH (more than 30 mm); 5) sustained or non-sustained ventricular tachycardia (VT); and 6) attenuated blood pressure response to exercise. [12] Death as a consequence of stroke, usually embolic and associated with atrial fibrillation, was virtually confined to much older patients. These 6 risk factors have low positive predictive value but high negative predictive value, although, even in the absence of conventional risk factors, hypertrophic cardiomyopathy patients have a low but non-trivial annual mortality risk of 0.6%.[12]

Sudden death in patients with HCM who practice competitive sports may be explained by the hypothesis that high-intensity sports may cause a massive activation of preganglionic sympathetic nerves that induce the release of catecholamines from the adrenal gland. When this increased amount of catecholamine reaches its receptors on the heart it can cause a significant ventricular ectopy, leading to bidirectional ventricular tachycardia, polymorphic ventricular tachycardia or ventricular fibrillation. [12,13] Therefore, high-intensity sports participation may act as an independent risk factor, even in the absence of conventional risk markers intrinsic to the disease process. [12]

Deaths caused by HCM are common in start-stop sports, for example, football and basketball. It is hypothesized that the combination of myocardial hypertrophy, impaired myocardial relaxation, myocardial ischemia, and dynamic left ventricular (LV) outflow obstruction impede augmentation of stroke volume for prolonged periods, and individuals with HCM are therefore usually selected out of endurance sports. [3] HCM-related deaths have been reported not only in competitive athletics but also during recreational activities.[12]

As for diagnosis, although more than 90% of affected individuals have an abnormal resting electrocardiogram, ECG is unreliable. [3] The diagnosis is made by recognition of the characteristic disease phenotype, that is, LVH without chamber dilatation in the absence of another cardiac or systemic disease capable of producing the magnitude of hypertrophy evident. Neither systolic anterior motion of the mitral valve, hyperdynamic LV function, or identification of pathogenic sarcomere mutations is obligatory for the clinical diagnosis of HCM.[15]

With the hypothesis that intense physical activity could provoke sudden cardiac death in hypertrophic cardiomyopathy and, conversely, limiting such activity could mitigate that risk, sports participation has been strongly discouraged in scientific guidelines published by the ACC in the years 1985, 2005, and 2015. [12] According to current United States guidelines, athletes with a probable or unequivocal phenotypic expression of hypertrophic cardiomyopathy should not participate in most competitive sports, with the exception of those of low intensity (class IA sports) (attachment 1) (Class III; Level of Evidence C). [15] Participation in competitive athletics by asymptomatic, genotype-positive hypertrophic cardiomyopathy patients without evidence of left ventricular hypertrophy by two-dimensional echocardiogram or cardiac magnetic resonance (MR) imaging is reasonable, particularly in the absence of a family history of hypertrophic cardiomyopathy-related sudden death (Class IIa; Level of Evidence C). [15] The ESC guidelines published in 2014 suggest that patients with HCM should avoid competitive sports activities, however, they should maintain a healthy lifestyle with recreational exercise, which should be tailored to symptoms and the risk of disease-related complications. [16]

Even with risk stratification, pre-participation screening and sports restriction, sudden cardiac death in HCM cannot be completely prevented. Restriction of all patients with HCM from vigorous or competitive activity may possibly be excessive. This strategy also does not eliminate playground deaths or deaths associated with minimal exertional activity in HCM and there are, as well, studies that demonstrate that a substantial proportion of patients with hypertrophic cardiomyopathy continue to compete at a high-intensity level, perhaps against medical advice without adverse clinical events. [17]

Arrhythmogenic Right Ventricular Dysplasia

ARVD is an inherited disease, usually with an autosomal dominant trait, but with some recessive forms also described. [4,18] However, the disease it not fully penetrant, which means that some people do not display the phenotype despite harbouring the pathogenic mutation. [19]

Its prevalence in general population ranges from 1/1,000 to 1/5,000, it is more common in males (3 to 1) and it is a leading cause of SCD in young athletes. [4,6,18,20]

ARVD is caused by mutations in genes encoding cardiac desmossomal proteins.[21] The desmosomal complex is crucial for cellular adhesion, tissue strength and stability.[18] This mutations cause disruption of the desmosome, which is responsible for the replacement of cardiac myocytes by fibro-fatty tissue, particularly in the right ventricle (RV), leading to a propensity to VT or ventricular fibrillation (VF) and an increased risk of sudden cardiac death, especially in young individuals and athletes. [4,20]

Patients usually present symptoms during the second to fifth decades of life, the typical are palpitations, arrhythmic syncope, and sudden cardiac arrest, which typically occurs in athletes.[18,20] Macroscopic appearances include RV dilatation, dysfunction, and aneurysm formation. The risk factors for developing SCD are previous cardiac arrest, unexplained syncope, chest pain with or without rise in cardiac biomarkers, VT with hemodynamic compromise and extensive structural disease including LV involvement, precordial T-wave inversions beyond V1 after puberty. [18]. In the presence of any of these risk factors, prophylactic implantable cardiac defibrillator (ICD) implantation should be taken into consideration. [4]

Four disease phases have been proposed: 1. Concealed phase: patients are asymptomatic and structural abnormalities are absent. SCD due to VF can be the primary manifestation in this phase; 2. Occurrence of symptomatic arrhythmias; 3. Early heart failure symptoms; 4. End-stage heart failure. [22]

Nonetheless, genetic mutations cannot entirely account for phenotypic expression and disease progression. On one hand, some patients with ARVD are genotype elusive (genetic mutations could not be identified, although they may be present), on the other, the pathogenic mechanisms remain unclear with epigenetic and environmental factors, such as exercise, that seem to play a vital role as disease modifiers. [18] The risk of ventricular arrhythmia is increased by exercise, and exercise training itself may promote

earlier disease manifestation and accelerate phenotypic expression of ARVD [6]: it is proposed that increased myocardial strain accelerates disruption of the desmosomes, resulting in fibro-adipose replacement (adverse remodelling), which increases the risk of arrhythmias and sudden death.[18,20]

Studies relating ARVD and SCD have come to some interesting conclusions: There is a fivefold risk of athletes dying of ARVD compared with non-athletes [4]; Patients engaged in competitive exercise had an earlier presentation of the disease and also had a twofold increase in the risk of life-threatening arrhythmias and death when compared with inactive patients and those practising only recreational sports [20]; Endurance athletes became symptomatic at an earlier age and had worse survival from ventricular arrhythmias and heart failure. Furthermore, patients who continued to participate in competitive exercise had worse survival compared with individuals who reduced their exercise after presentation [23]; A recent study assessed the safety of the American Heart Association minimum exercise recommendations for healthy desmosomal mutation carriers. There were no life-threatening ventricular arrhythmias in the healthy carriers who restricted exercise to the upper bounds of the minimum exercise recommendations[24]

These studies lead to the conclusion that high-level physical activity promotes disease onset, progression and adverse outcome. [25] Therefore, the identification of affected athletes by pre-participation screening can help to substantially reduce mortality in this cohort.[18]

Clinical diagnosis can be challenging but relies largely on correctly identifying symptoms, family history and genetics, and by correlating them with electrocardiogram (ECG) and imaging tools. The ECG is important to assess for depolarisation and repolarisation abnormalities, such as T-wave inversion in precordial leads V1 through V3 (most common ECG abnormality), left bundle-branch pattern ventricular tachyarrhythmia, and epsilon waves. Echocardiography and cardiac MR can detect functional and structural alternations, such as right ventricular dilation or segmental wall motion abnormalities, aneurysm formation, or fatty deposition in the right ventricular wall, that often only become visible after electrical alterations like premature ventricular beats, VF and VT. [15,18] Abnormal findings are then separated into major and minor criteria and patients are classified with diagnosis, borderline or possible ARVD (attachment 2).[15]

It is recommended that patients with a definite, borderline or possible diagnosis of ARVD do not participate in competitive and/or endurance sports. Furthermore, they should be restricted from participation in athletic activities, with the possible exception of recreational low intensity sports (Class III; Level of Evidence C).[15,24,26]

Athletes with borderline or possible ARVD, as well as those who are genotype positive–phenotype negative, should receive continued follow-up, because ARVD may progress phenotypically, and become more clinically apparent with time. [15]

The treating physician should keep in mind that ARVD cannot be excluded by the absence of structural abnormalities, as arrhythmias often occur in the early "concealed phase", preceding structural abnormalities, however, most patients with ventricular arrhythmias will show structural changes. [20] Furthermore, adaptation of the RV to increased workload in endurance athletes can mimic ARVD, and there is a debatable grey zone of what is considered physiological adaptation that may lead to more difficult diagnosis based on the phenotype.[18]

After establishing an accurate diagnosis, the goals of ARVD management are prevention of sudden cardiac death, minimising arrhythmias and device therapies, and preventing the progression of the disease. [20]

Therapeutic strategies include restriction from endurance and competitive sports, b-blockers, antiarrhythmic drugs, heart failure medication, implantable cardioverter-defibrillators and endocardial/epicardial catheter ablation.[18]

Congenital and Acquired Coronary Artery Anomalies

Congenital or acquired coronary artery abnormalities are reportedly the cause of SCD in around 1/5 of athletes. [4,6,27]

Congenital Coronary Artery Anomalies

Congenital coronary artery anomalies (CCAA) are modifications of their origin, course or structure and its incidence varies between 0,2 and 5,6% of the general population. Although the majority is asymptomatic, they are the second leading cause of sudden cardiac death in young athletes occurring in ≈17% of cases.[28] Anomalous origins of coronary arteries from the wrong sinus of Valsalva or from the pulmonary artery are estimated to be present in ≈1% of the overall population but are proportionately far more

common in athletes who die suddenly. The most common anomalous origin is the right coronary artery originating from the left sinus of Valsalva, but among athletes who have died suddenly, anomalous origin of the left main or left anterior descending coronary artery from the right sinus of Valsalva is far more prevalent. Furthermore, SCDs are most strongly associated with the pattern in which the anomalous left coronary artery passes between the aorta and main pulmonary artery. An anomalous origin of a coronary artery from the pulmonary artery is far less commonly observed in athletes who die suddenly and in fact often presents with myocardial infarction in infancy or early childhood.[29]

The ECG is an unreliable screening tool for suspecting or recognizing anomalous origin of coronary arteries before an event, and even stress tests are not uniformly positive among people with these anomalies. Clinical symptoms, such as exertional chest discomfort or dyspnea, may be helpful, but some reports suggest that 50% of SCDs associated with coronary artery anomalies were first events without prior symptoms. The best methods for identifying the anomaly include coronary angiography (CA), computed tomography (CT) angiography and MR angiography. Although not uniformly successful, athletes undergoing echocardiographic studies for any reason should have careful attempts to identify the origins of the coronary arteries. Surgical procedures are the only therapies available for correcting these anomalies.[29]

1. *Anomalous origin of the coronary artery from the opposite sinus of Valsalva with an interarterial course*

The most common anomalies implicated are left coronary artery origins in the right sinus of Valsalva and right coronary artery origins in the left sinus of Valsalva. [27]

Anomalous origin of the coronary artery from the opposite sinus of Valsalva is usually harmless and not detected during life. However, if the anomalous coronary artery courses between the pulmonary artery and the aorta (interarterial), SCD may occur during or shortly after vigorous exercise: the coronary artery may arise from the aortic root at an acute angle and with a slit-like orifice and this can potentially compromise coronary blood flow. In addition, it may also contain a narrowed intramural – inside the aortic wall – segment. During vigorous exercise, the combination of an increased oxygen demand, decreased blood supply to the myocardium caused by the narrow coronary artery segment, additional narrowing of the coronary artery due to the dynamic state of the aorta and a

shorter diastolic period may result in cardiac ischaemia, ventricular arrhythmias, and sudden cardiac death. [4, 27]

Diagnosis using ECG, echocardiography, and exercise stress testing is notoriously difficult because affected individuals rarely reveal features of inducible ischemia during exercise stress testing or pharmacological functional tests. The presence of anomalous coronary artery arising from the opposite sinus of Valsalva has been detected by echocardiogram as an incidental finding. By echocardiographic screening, the estimated prevalence rate of anomalous origin of a right or left coronary artery from the opposite sinus of Valsalva is probably around 0.1–0.2% in the general population; however, using magnetic resonance angiography as the screening tool, which is more precise, the prevalence rate is higher (0.7%). For this reason, cardiac magnetic resonance angiography and computed tomography coronary angiography are the gold standard imaging modalities to confirm the diagnosis and to delineate the detailed coronary artery anatomy. [4,27]

As SCD usually occurs only during strenuous exercise, many experts believe that patients diagnosed with this condition should avoid vigorous sports. [27]

Victims of SCD due to CCAA are often asymptomatic before presentation, although chest pain associated with syncope should raise suspicion of the disorder. [4]

Symptomatic patients with evidence of ischaemia should have surgical correction. No treatment is needed for asymptomatic patients with an anomalous right coronary artery from the left sinus of Valsalva. [4,27]

Athletes with an anomalous origin of a right coronary artery from the left sinus of Valsalva should be evaluated by an exercise stress test. Those who exhibit symptoms, arrhythmias, or signs of ischemia on exercise stress test should be restricted from participation in all competitive sports, with the possible exception of class IA sports, before a surgical repair. Those without either symptoms or a positive exercise stress test, permission to compete can be considered after adequate counselling of the athlete and/or the athlete's parents (in the case of a minor) as to risk and benefit, taking into consideration the uncertainty of accuracy of a negative stress test (Class IIa; Level of Evidence C).[29]

Athletes with an anomalous origin of a left coronary artery from the right sinus of Valsalva, especially when the artery passes between the pulmonary artery and aorta, should be restricted from participation in all competitive sports, with the possible exception of class IA sports, before surgical repair. This recommendation applies whether the anomaly is identified as a consequence of symptoms or discovered incidentally (Class III; Level of Evidence B).[29]

2. *Anomalous left coronary artery from the pulmonary artery*

Anomalous left coronary artery from the pulmonary artery is a rare form of congenital heart disease occurring in about 1/300,000 live births. It is usually detected in infancy at 2–3 months of age when the patient presents with poor feeding and irritability, but in some cases patients can develop adequate collateral circulation from the right coronary artery in the newborn period, remaining asymptomatic only to manifest in adulthood with myocardial ischaemia, ventricular arrhythmias, and SD. [27]

The chest X-ray usually shows evidence of heart failure with cardiomegaly and pulmonary edema. The electrocardiogram shows signs of myocardial ischaemia or infarction. An echocardiogram reveals a dilated LV with myocardial dysfunction and often severe mitral regurgitation. The anomalous left coronary artery is seen arising from the pulmonary artery with a reversed Doppler flow pattern. [27]

Athletes with this CCAA can participate only in low-intensity class IA sports, whether or not they have had a prior myocardial infarction (Class I; Level of Evidence C).[29]

3. *Coronary artery ostial disease*

An ectopic location of a coronary artery ostium can result in progressive coronary artery ostial stenosis or atresia. This rare congenital heart defect may not be recognised until later in life and may cause exercise-induced chest pain, palpitations, or SCD due to ventricular arrhythmias. [27]

Acquired Coronary Artery Anomalies

Acquired coronary artery abnormalities can occur in Kawasaki disease, Ehlers–Danlos syndrome, Marfan syndrome, Takayasu arteritis, polyarteritis nodosa, scleroderma, neurofibromatosis, dyslipidaemias, and systemic lupus erythematous. Of these, Kawasaki disease is the leading cause of acquired coronary artery disease in children.[27]

1. *Kawasaki Disease*

The cause of Kawasaki disease (KD) is still unknown, but there is a significant difference in incidences according to ethnic group, demonstrated by the bigger incidence in children with Japanese ancestry. This condition can result in inflammatory myocarditis and small and medium sized blood vessel vasculitis. It mainly affects children <5 years of age, but the disease sequelae can extend into adulthood: aneurysms, stenosis and thrombosis lead to ventricular fibrillation and myocardial infarction, which is the main cause of death in patients with KD.[30] Giant coronary artery aneurysm can also lead to aneurysm rupture and SD. [27]

It is recommended that among patients who had had Kawasaki disease and moderate (4–8mm internal diameter) or giant (⩾8mm) aneurysms in infancy or childhood, lifelong, diligent follow-up with some combination of serial electrocardiograms, stress tests, and appropriate imaging studies to detect coronary artery abnormalities and myocardial ischaemia is necessary. Among those whose aneurysms resolved or in the presence of residual small aneurysm and when there is no coronary artery stenosis, sports participation is usually permitted. [27]

Aortic Dissection

Acute aortic dissection (AAD) of an ascending aortic aneurysm is an uncommon cause of sudden death in young athletes. Individuals at risk include those having a variety of conditions in which structural weakness of the ascending aorta predisposes to pathological dilation under prolonged periods of increased wall stress. These conditions include Marfan syndrome, Loeys-Dietz syndrome, bicuspid aortic valve, and the vascular form of Ehlers-Danlos syndrome. [31]

Marfan Syndrome

Cardiovascular characteristics in Marfan syndrome patients are caused by defects in the fibrillin-1 (*FBN1*) gene, encoding an extracellular matrix protein present in elastic tissues, such as the heart and blood vessels. [32] Increased blood pressure and aortic stress during intense physical exertion increases the risk for aortic dissection or rupture or may accelerate aneurysm formation. Athletes with Marfan syndrome should undergo echocardiographic (and in some instances MR or CT) measurement of the aortic root dimension every 6 to 12 months. It is reasonable for them to participate in low and

moderate static/low dynamic competitive sports (classes IA and IIA) if they do not have ≥1 of the following: [33]

a. Aortic root dilatation;

b. Moderate to severe mitral regurgitation;

c. LV systolic dysfunction (ejection fraction <40%);

d. Family history of aortic dissection at an aortic diameter <50 mm;

However, high intensity sports should be completely avoided (Class IIa; Level of Evidence C).

Diagnosis and Prevention

Pre-participation screening appears efficient in preventing SCD, since its usage has reduced the number of fatal events in sports, but the screening programs for athletes vary greatly in European countries and between Europe and the USA (attachments 3 and 4).[1,2]

According to the European guidelines, the screening protocol for an asymptomatic active adult changes according the intensity of exercise: low intensity does not require screening; Moderate intensity activity needs an assessment of risk by the person itself or someone non-physician. If the risk is considered negative, no further investigation is needed, but if the risk is positive then a screening by a physician is recommended. In high intensity activities, screening by a physician is always recommended: [1]

1. Personal history
    a. Syncopal episodes
    b. Palpitations
    c. Chest pain
2. Family history
3. Physical exam
4. Risk Score (attachment 5)
5. Rest ECG

Based on the results, athletes may be considered eligible for exercise training or appointed to further evaluation (echocardiography and/or cardiac MR, exercise test and others).[1]

As for the American Guidelines, they promote a pre-participation checklist for all athletes, but consider that limited data support their utility, cost and applicability. They recommend further investigation for patients that present one of the following in the pre-participation screening: [2]

1. Positive personal history
    a. Chest pain on exertion
    b. Unexplained fainting
    c. Excessive and unexplained fatigue associated with exercise
    d. Hearth murmur
    e. High blood pressure
2. Family history
    a. SD before the age of 50
    b. Inherited hearth diseases causes of SCD
3. Positive physical examination
    a. Hearth murmur
    b. Difference between radial/femoral pulse
    c. Physical appearance of Marfan syndrome
    d. High brachial artery blood pressure

This shows that the approach to detect the risk of sudden death in the athlete is not consensual in some aspects between the Europeans and the Americans, namely who to trace and how to do the screening.

As previously mentioned in the European recommendations, the type of approach to be performed depends on the level of intensity of the effort and an evaluation is justified in cases of physical activity requiring moderate or intense exertion. In the US recommendations the sudden death risk approach is reserved only for competitive athletes. [1,2]

The pool of athletes to screen is too big to allow a full investigation in all of them and the screening program has too much false-positive and false-negative results to be efficient to apply to every athlete. [1,2]

As so, we present an algorithm based on current guidelines and recommendations that helps to select those who can be eligible for exercise with little evaluation, and those who require further investigation.

The following algorithm is based on ACC/AHA recommendations and guidelines and on ESC guidelines: [1,2]

In order to consider an athlete eligible for exercise, the evaluation of an athlete should always be based on a careful clinical history, so that potential symptoms or suspicious personal or family history does not go unnoticed.

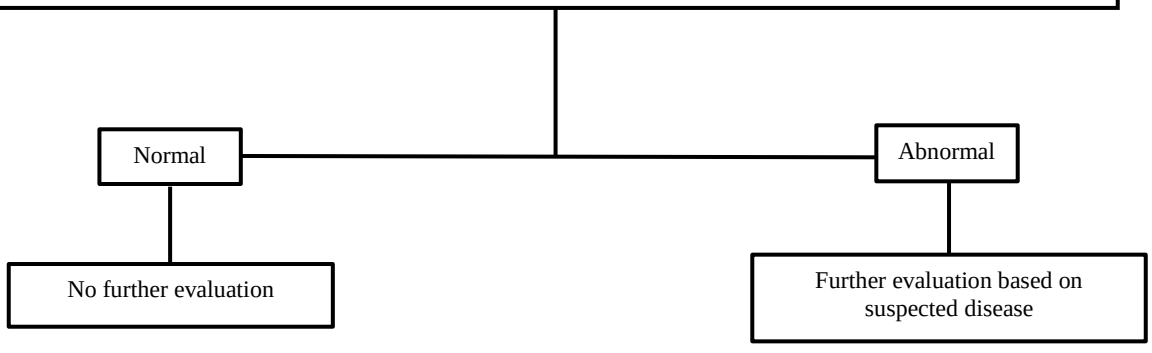
It is important to emphasize in the personal history the need to question whether there is: chest pain/discomfort on exertion, unexplained fainting or near-fainting, excessive and unexplained fatigue associated with exercise, high blood pressure or known cardiac condition.

In family history it is necessary to know if there is: evidence of death of one or more relatives due to a cardiac cause or the presence of genetic conditions with the potential to cause SCD, such as HCM, ARVD, Marfan Syndrome, Long-QT syndrome or others.

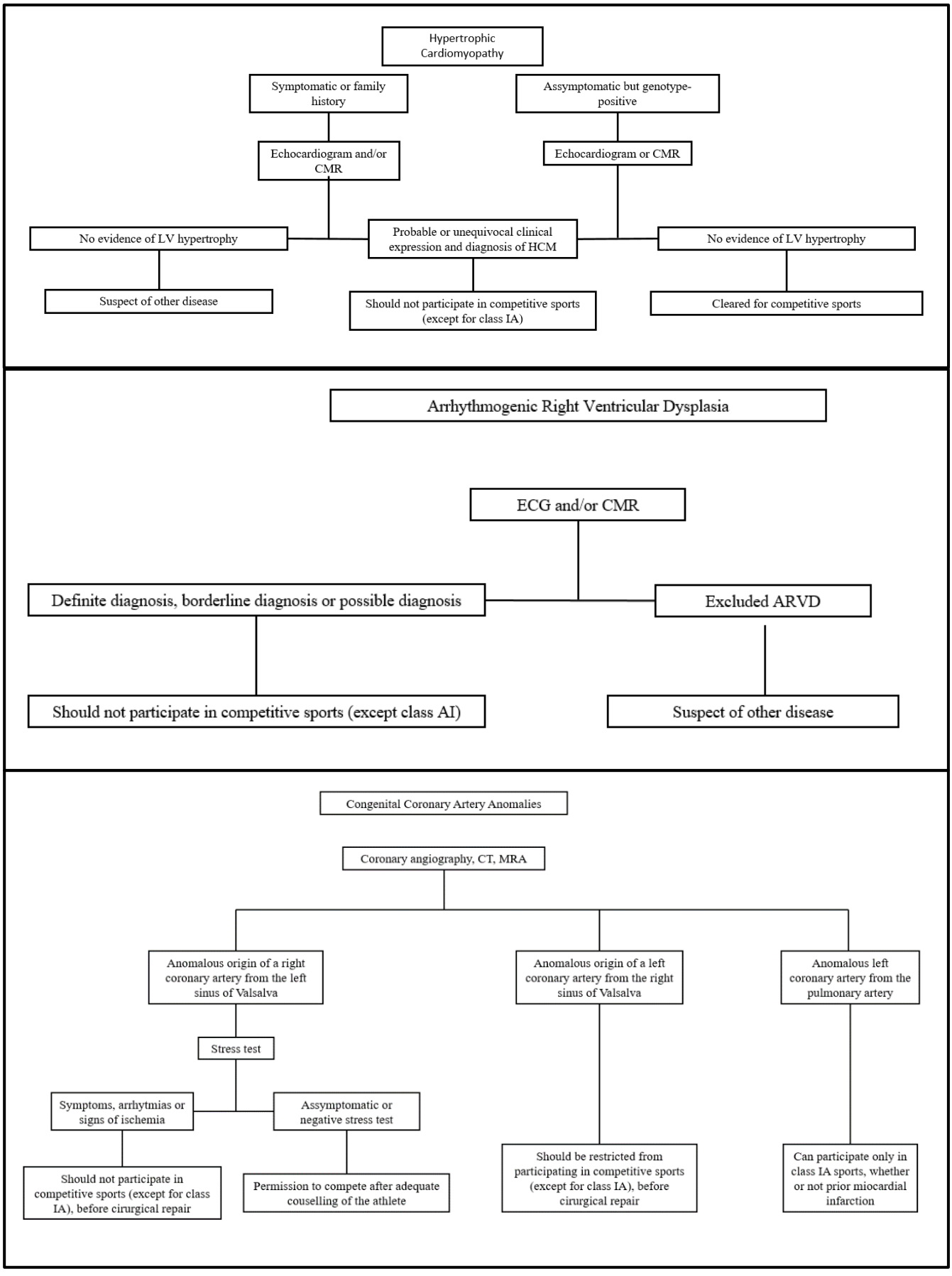
The physical examination should focus on physical appearance, cardiac evaluation, to try to identify a heart murmur, femoral/radial pulse comparison and measure of brachial blood pressure.

After this first evaluation, if everything is normal, than the athlete is considered eligible for competitive sports. If not, than further evaluation is needed based on the suspected disease.

1. Personal History
   - ✓ Symptoms/events related to arrhythmia:
     - ➢ Palpitations
     - ➢ Light-headedness
     - ➢ Syncope
     - ➢ Dyspnea
     - ➢ Chest pain
     - ➢ Cardiac arrest
     - ➢ Excessive and unexplained fatigue associated with exercise
   - ✓ Known heart disease (congenital or acquired)
   - ✓ Risk factors for heart disease
     - ➢ Hypertension
     - ➢ Diabetes Mellitus
     - ➢ Hyperlipidemia
     - ➢ Smoking
   - ✓ Medications:
     - ➢ Antiarrhythmic medications
     - ➢ Other medications with potential for QT prolongation and torsades de pointes
     - ➢ Medications with potential to provoke or aggravate Ventricular Arrhythmias
     - ➢ Stimulants including cocaine and amphetamines
     - ➢ Supplements including anabolic steroids
2. Family History
   - ✓ SCD, SCA, or unexplained drowning in a first-degree relative
   - ✓ SIDS or repetitive spontaneous pregnancy losses (association with cardiac channelopathies)
   - ✓ Genetic conditions with the potential to cause SCD
     - ➢ HCM
     - ➢ ARVD
     - ➢ Marfan syndrome
     - ➢ Long-QT syndrome
     - ➢ Arrhytmias
     - ➢ Conduction disorders
3. Examination
   - ✓ Physical appearance
   - ✓ Hearth rate and regularity
   - ✓ Blood pressure
   - ✓ Jugular venous pressure
   - ✓ Murmurs
   - ✓ Pulses
   - ✓ Edema
   - ✓ Sternotomy scars



Adapted from American Heart Association and American College of Cardiology Recommendations and Guidelines and European Society of Cardiology Guidelines



Adapted from American Heart Association and American College of Cardiology Recommendations and Guidelines and European Society of Cardiology Guidelines

Conclusions

SDC is a very traumatic event that usually occurs in apparently healthy athletes, which causes a large emotional and social impact on the surrounding community.

The main causes have already been identified, with HCM being the most predominant condition, but the problem remains the difficulty of the diagnosis, most diseases are indolent and the first manifestation is often SD and there is no consensus on how to select athletes that can take part in sports and those who should be recommended to stop practicing. An exception are class IA sports, which do not seem to have any restriction, independently from the underlying condition.

The algorithm presented is based on current recommendations and guidelines from both Europe and the USA and is aimed to help in a better assessment of the athlete's future.

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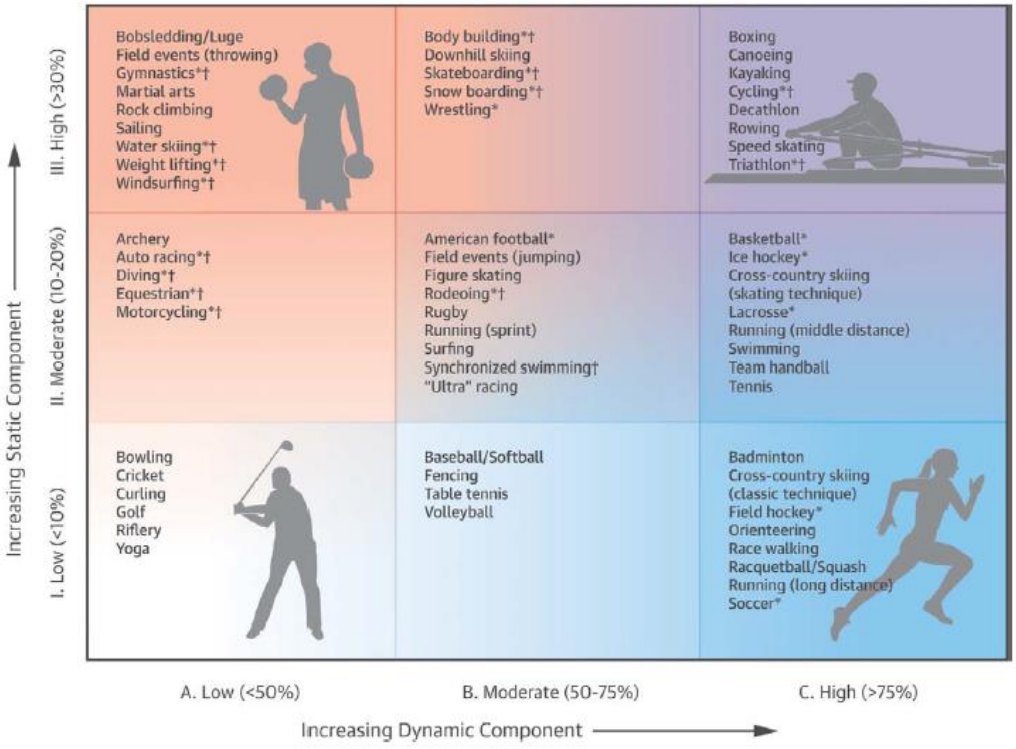
Attachment 1 – Classification of Sports: Dynamic, Static, and Impact [34]



Attachment 2 – ARVD diagnosis criteria[35]

REVISED TASK FORCE CRITERIA

I. Global and/or Regional Dysfunction and Structural Alterations*

- **Major (by 2D echo)**

Regional RV akinesia, dyskinesia or aneurysm.

And one of the following (end diastole):

Parasternal long axis view RVOT (PLAX)	≥ 32 mm
Corrected for body size (PLAX/BSA)	≥ 19 mm/m^2
Parasternal short axis view RVOT (PSAX)	≥ 36 mm
Corrected for body size(PSAX/BSA)	≥ 21 mm/m^2
or	
Fractional area change (FAC)	≤ 33%

- **Major (by MRI)**

Regional RV akinesia or dyskinesia or dyssynchronous RV contraction

And one of the following:

Right ventricular end diastolic volume (RVEDV/BSA)	≥110 ml/m^2 male
	≥100 ml/m^2 female
OR	
Right ventricular ejection fraction (RVEF)	≤40%

- **Major (by RV angiography)**

Regional RV akinesia, dyskinesia or aneurysm

- **Minor (by 2D echo)**

Regional RV akinesia or dyskinesia

And one of the following (end diastole):

Parasternal long axis view RVOT (PLAX)	≥ 29 - < 32 mm
Corrected for body size (PLAX/BSA)	≥ 16 - < 19 mm/m^{2i}

Attachment 2 (continuation)

Parasternal short axis view RVOT (PSAX)	≥ 32 - < 36 mm
Corrected for body size (PSAX/BSA)	≥ 18 - < 21 mm/m^2
or	
Fractional area change (FAC)	> 33% - ≤ 40%

- **Minor (by MRI)**

Regional RV akinesia or dyskinesia or dyssynchronous RV contraction

And one of the following:

Right ventricular end diastolic volume/BSA	≥100 - < 110 ml/m^2 male
	≥90 - < 100 ml/m^2 female
OR	
Right ventricular ejection fraction (RVEF)	> 40% - ≤ 45%

II. Tissue Characterization of Wall

- **Major**

Residual myocytes <60% by morphometric analysis, (or < 50% if estimated), with fibrous replacement of the RV free wall myocardium in at least 1 sample, with or without fatty replacement of tissue on endomyocardial biopsy.

- **Minor**

Residual myocytes 60 – 75% by morphometric analysis, (or 50 to 65% if estimated), with fibrous replacement of the RV free wall myocardium in at least 1 sample, with or without fatty replacement of tissue on endomyocardial biopsy.

III. Repolarization Abnormalities

- **Major**

Inverted T waves in right precordial leads (V_1, V_2 and V_3) or beyond in individuals > 14 years of age (in the absence of complete right bundle branch block QRS ≥ 120 msecs).

- **Minor**

Inverted T waves in leads V_1 and V_2 in individuals > 14 years of age (in the absence of complete right bundle branch block), or in V_4, V_5, or V_6.

Inverted T waves in leads V_1, V_2, V_3 and V_4 in individuals > 14 years of age in the presence of complete right bundle branch block.

IV. Depolarization/Conduction Abnormalities

- **Major**

Attachment 2 (continuation)

Epsilon wave (reproducible low amplitude signals between end of QRS complex to onset of the T wave) in the right precordial leads (V_1 to V_3)

- **Minor**

Late potentials by signal averaged ECG in at least one of three parameters in the absence of a QRS duration of ≥110 msecs on the standard ECG.

Filtered QRS duration (fQRS)	≥114 msecs
Duration of terminal QRS < 40 μV (LAS)	≥38 msecs
RMS voltage of terminal 40 msecs	≥20 μV

Terminal activation duration of QRS ≥ 55ms measured from the nadir of the S wave to the end of the QRS, including R', in V_1, V_2 or V_3, in the absence of complete right bundle branch block.

V. Arrhythmias

- **Major**

Non-sustained or sustained VT of left bundle branch morphology with superior axis (negative or indeterminate QRS in II, III, AVF and positive in AVL)

- **Minor**

Non sustained or sustained VT of right ventricular outflow configuration, LBBB morphology with inferior axis (positive QRS in II, III, AVF and negative in AVL) or of unknown axis.

Greater than 500 ventricular extrasystoles/24 hours by Holter

VI. Family History

- **Major**

ARVC/D confirmed in a first-degree relative who meets current task force criteria.

ARVC/D confirmed pathologically at autopsy or surgery in a first degree relative.

Identification of a pathogenic mutation [†] categorized as associated or probably associated with ARVC/D in the patient under evaluation.

- **Minor**

History of ARVC/D in a first degree relative in whom it is not possible or practical to determine if the family member meets current task force criteria.

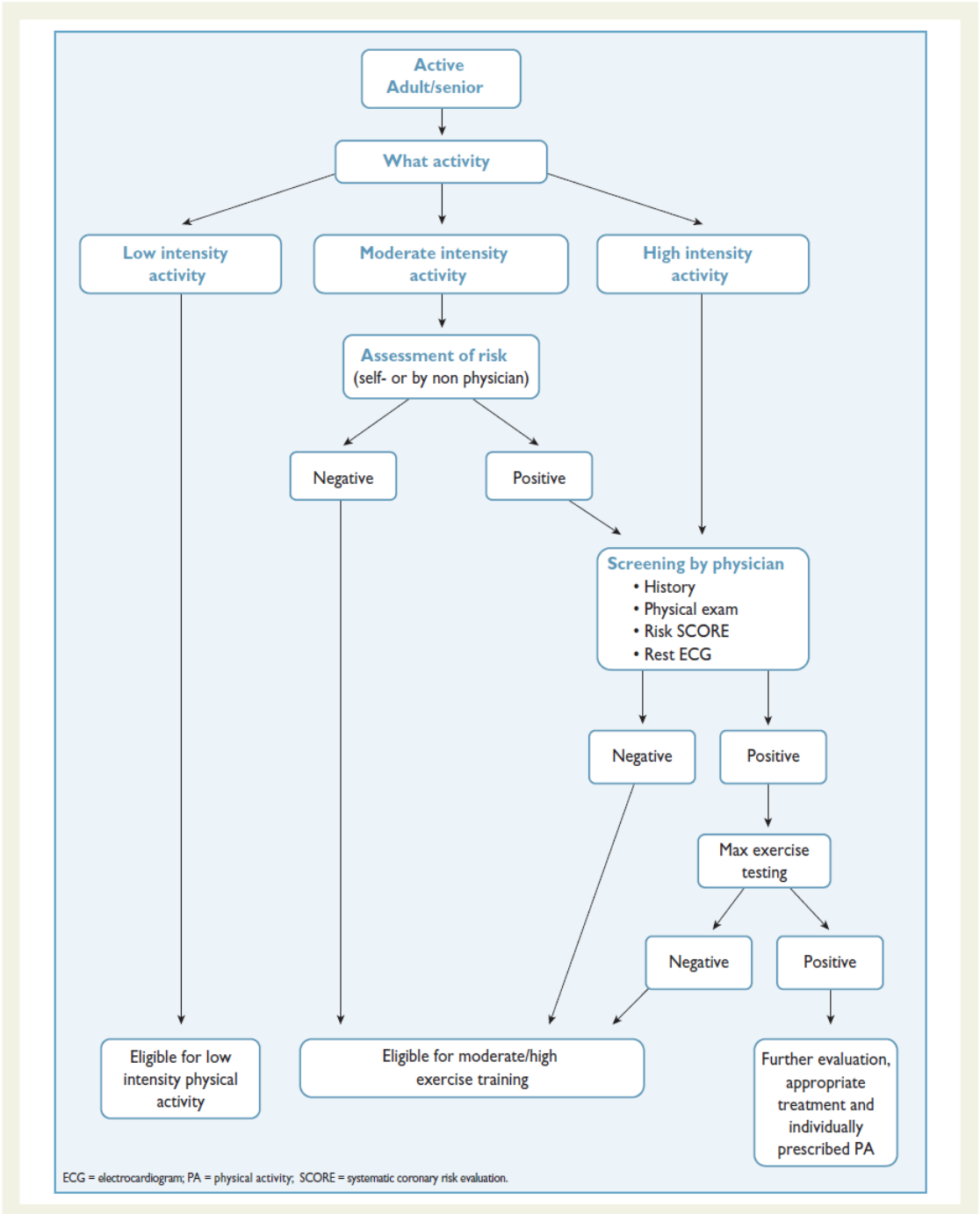
Premature sudden death (<35 years) due to suspected ARVC/D in a first degree relative.

ARVC/D confirmed pathologically or by current Task Force Criteria in second degree relative.

Diagnostic terminology for revised criteria

- Definite diagnosis: 2 major or 1 major and 2 minor criteria or 4 minor from different categories
- Borderline: 1 major and 1 minor or 3 minor criteria from different categories
- Possible: 1 major or 2 minor criteria from different categories

Attachment 3 – ESC proposed pre-participation evaluation protocol for asymptomatic active adult [1]



Attachment 4 – AHA recommendations for pre-participation cardiovascular screening of competitive athletes [2]

Medical History
Personal history
1. Chest pain/discomfort on exertion
2. Unexplained fainting or near-fainting
3. Excessive and unexplained fatigue associated with exercise
4. Heart murmur
5. High blood pressure
Family history
6. ≥1 relatives who died of heart disease (sudden/unexpected or otherwise) before age 50 years
7. Close relative <50 years of age with disability from heart disease
8. Specific knowledge of certain cardiac conditions in family members: hypertrophic or dilated cardiomyopathy, in which the heart cavity or wall becomes enlarged; long-QT syndrome, which affects the heart's electrical rhythm; Marfan syndrome, in which the walls of the heart's major arteries are weakened; or clinically important arrhythmias or heart rhythms
Physical examination
9. Heart murmur
10. Femoral pulses to exclude narrowing of the aorta
11. Physical appearance of Marfan syndrome
12. Brachial artery blood pressure (taken in a sitting position)

Attachment 5 – ESC cardiovascular risk score [1]